Remarks/Arguments

In the specification, the paragraphs 38 and 40 have been amended to correct minor clerica errors.

Claims 1, 6-9, 11, 15-17 and 21-34 remain in this application. Claim 34 has been amended.

Claim Rejections – 35 U.S.C. §112

Claims 1, 6-9, 11, 15-17 and 21-34 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "extrusion aid" was stated to render the claim indefinite and it was also stated that the specification does not provide a standard for ascertaining the requisite degree. The Applicant respectfully disagrees with the Examiner. The term "extrusion aid" is well known in the pharmacological sciences and is described for example in the attached document (FMC Corporation, Product Brochure 2003). Here Avicel PH™ (microcrystalline cellulose) is clearly described as an extrusion aid. Furthermore, it has now been clarified in the description in paragraphs 38 and 40 that the microcrystalline cellulose is an extrusion aid and was inadvertently listed as a compression aid. One of skill in the art would readily understand what an extrusion aid is and what type of material would be a selected as an extrusion aid. Furthermore, the application need not teach what is known in the art.

Claim Rejections - 35 U.S.C. § 103

Claims 1, 6-9, 17, 21, 23, 26 and 30-33 are rejected under 35 U.S.C. § 103 as being unpatentable over Cheng on record. The Examiner asserts that Cheng teaches an extended time release formulation comprising 50-98% antihyperglycemic drug which is formulated as a tablet and encased in a semi-permeable polymer film layer. The Examiner states that the membrane is soluble at pH 7.5 and is made of 50-99% cellulose esters or methacrylic acid copolymer comprising PEG, plasticizers and excipients. The Examiner contends that the Applicant does not show unexpected data for Cheng's coating having 49% polymer.

The Applicant respectfully disagrees with the Examiner. Cheng teaches a core of active that is coated with a semi-permeable membrane. The semi-permeable membrane is stated to be permeable to the passage of an external fluid such as water and biological fluids and is

impermeable to the passage of the drug in the core (column 4, lines 10-16). As such, the semi-permeable membrane does not dissolve but rather remains intact at alkaline pH and during transit in the gastrointestinal tract. Again, the membrane is not pH reactive. This is because Cheng uses different polymers to that presently claimed. It is stated in column 4 that the materials useful in forming the semi-permeable membrane are "cellulose esters, cellulose diesters,.....The most preferred semi-permeable membrane material cellulose acetate comprising an acetyl content of 39.3 to 40.3%". The semi-permeable membrane may further comprise a flux-enhancing agent such as PEG and methacrylic acid copolymers. As indicated in the attached excerpt from Eastman Chemical Company 1995, cellulose esters may be enteric or non-enteric. Non-enteric cellulose esters are semi-permeable and are represented for example by cellulose acetate which is the preferred polymer taught by Cheng.

In contrast, the presently claimed encasement coat comprises 5 up to less than about 50% by weight polymer and PEG. The polymer is stated in paragraph 12 of the present application that the composition of the invention is not a controlled release pharmaceutical tablet comprising a semi-permeable coating membrane surrounding the core with passageways in the membrane. Furthermore, the description clearly teaches that the polymeric film is soluble in a pH of about above 5.0 which is recited in the present claims. This is not taught or suggested by Cheng. Cheng's semi-permeable coating is not pH dependent at all. The teaching of dissolution at pH 7.5 in Cheng refers to the pH of the various fluids used in the dissolution studies. Again, the fluid passes through the semi-permeable membrane to the core which then enable the dosage form to dispense all of the drug through the passageway and/or the porous membrane (column 4, lines 30-34). Cheng's formulation works differently as discussed *supra* and this is because Cheng teaches the use of non-enteric cellulose esters and other non-dissolving polymers. As a result, Cheng's formulation provides a different release profile of the drug as is shown in the attached declaration by co-inventors Dr. Amina Odidi and Dr. Isa Odidi. The declaration provides dissolution data between a model drug using the presently claimed formulation versus that taught by Cheng. As is seen in the graph, the release of the drug using the presently claimed formulation is initially much more rapid which peaks and then provides a consistent level of release over several hours. In contrast, the Cheng formulation exhibits an initial slow dissolution which does not peak for several hours.

To summarize, Cheng does not teach or suggest an encasement coat comprising one or more layers of a polymeric film encasing said pharmaceutical active, where the encasement coat is soluble in a pH of above about 5.0 and comprising about 5 up to less than 50% by weight polymer and about 0.5%-30% by weight plasticizer of polyethylene glycol. As such, the claimed polymer is not semi-permeable but rather a soluble polymer as is further specified in claim 9 or 21 for example. Furthermore. Cheng is silent with respect to the teachings of using shellac or zein as recited in claim 11.

To conclude, Cheng does not teach or suggest the claimed formulation having the release profile as presented in the attached declaration.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,
SIM & MCBURNEY

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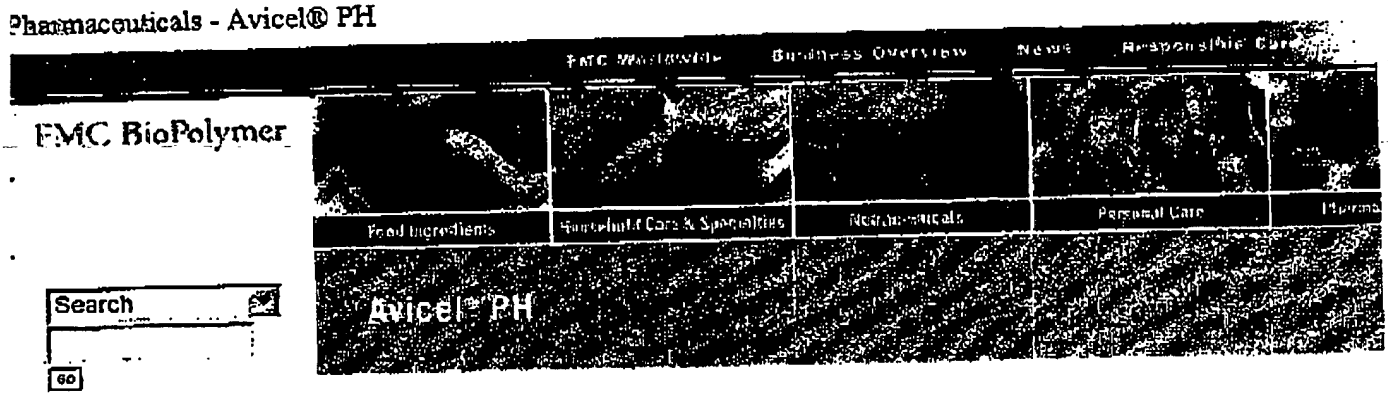

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Avicel PH Introduction

Avicel PH is the original microcrystalline cellulose (NF, Ph.Eur., BP, JP) which enabled large scale conversion to direct compression tablet manufacture in the pharmaceutical industry. This revolutionized the industry and brought new levels of efficiency to commercial tablet production. The pharmaceutical industry continues to benefit from FMC BioPolymer's innovat as modern Avicel PH grades are now available to boost productivity even further. Large-particle Avicel PH-200 enables production to maximize tablet press speed due to its superior flowability. High density grades (Avicel PH-301 and Avicel PH-302) not only improve flow and production rates, but enable larger batch size due since they occupy less volume in key piece production equipment. No matter what your formulation challenge, we have the perfect grade of Avicel for you. Only Avicel I is backed by FMC BioPolymer's worldwide capabilities in manufacturing, technical service, sales and supply chain. Our dual service, and reliability are unparalleled in the industry. For all of these reasons, Avicel PH is the standard to which all other pharmaceutical excipients are compared.

Applications

Direct Compression, Dry Granulation, Wet Granulation, Extrusion-Spheronization, Encapsulation

Benefits

Over the years, Avicel PH has earned its place in countless solid dosage formulations, thanks to its proven consistency and ability to perform many functions. It is the excipient of choice for direct compression formulations, lending superior compactib and carrying capacity to tablets. Avicel PH is self-lubricating and promotes rapid disintegration. These properties also benefit granulation processes such as roller compaction or slugging. In addition to acting as an auxiliary binder in wet granulation, Avicel PH helps control the wet mass consistency, reduces screen blockage, and promotes uniform, rapid drying. Avicel PH an essential extrusion-spheronization aid, contributing plasticity to the wet mass in-process while imparting strength to the finished pellet. When included in capsule formulations, Avicel PH improves flow, facilitates plug formation and aids capsule disintegration.

Direct Compression: Make high bulk density Avicel PH-302 or large particle size Avicel PH-200 your preferred cho for direct compression formulations and reap the benefits of increased productivity. Both grades offer flow improvements ov the standard Avicel grades. Avicel PH-200 enables the maximum flow, delivering minimum weight variation and excellent content uniformity. The increased density of Avicel PH-302 imparts fast flow as well as the potential to increase production b size in existing pharmaceutical processing equipment. If you are with coarse, granular, crystalline, or otherwise difficult to compress materials, consider Avicel PH-105. With its very fine particle size and resultant increase in surface area, this grad offers superior compressibility. Avicel PH-105 is often admixed with standard Avicel PH grades in order to achieve desired fl properties.

Moisture Sensitive Drugs: FMC offers three specialized grades of Avicel PH with a varying moisture conten and particle size. Look to Avicel PH-112, Avicel-PH-103, and Avicel PH-113 to help extend shelf-life and improve stability of moisture-sensitive formulations.

Wet Granulation: Avicel PH-101 is the logical choice for intragranular incorporation as it ensures faster and more trou free processing. Avicel PH promotes rapid, even wetting; speeds drying; reduces screen blockage; minimized case hardenir controls dye migration; and promotes disintegration. Post granulation addition of Avicel PH imparts all of the usual direct compression advantages. Consider high density Avicel PH-301 or PH-302 as well as Avicel PH-102 as additions to the runn mix to improve flow and compactibility during compression.

Encapsulation: Look to our high density Avicel PH-301 and PH-302 grades to optimize your capsule filling operations Enhanced flowability results in improved productivity and lower capsule weight variation. Higher density grades occupy less volume in your capsule formulation, leaving precious room for active ingredients.

Detailed Product Descriptions

PRODUCT SPEC SHEETS AVAILABLE: Avicel PH 101, 102, 103, 105 112, 113,200, 301, 302

Pharmaceuticals - Avicel® PH

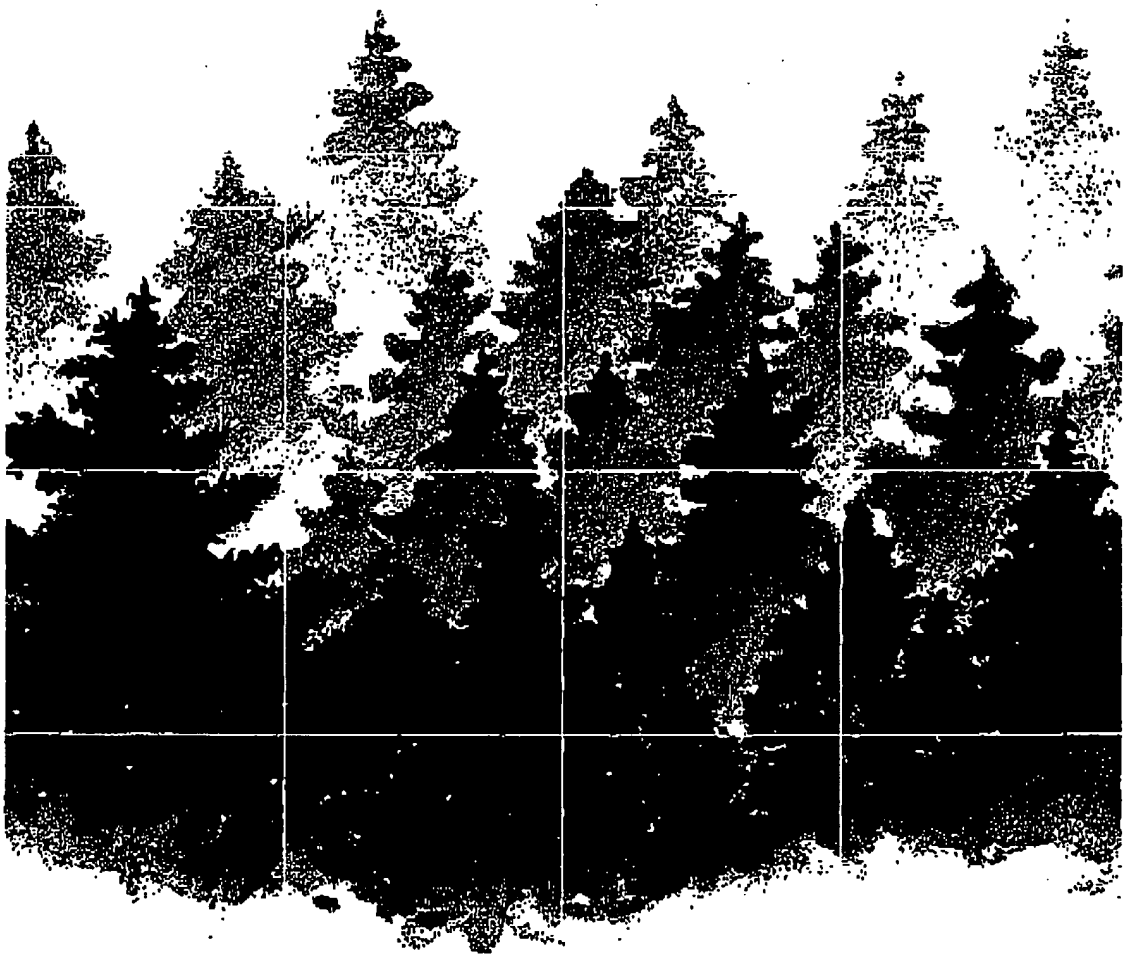
MSDS

Available by contacting FMC BioPolymer.

Eastman

Cellulose Esters

for Pharmaceutical Drug Delivery



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Material Safety Data Sheets providing safety precautions that should be observed in handling and storing Eastman products are available on request. You should obtain and review the available material safety information before handling any of these products. If any materials are mentioned that are not Eastman products, appropriate industrial hygiene and other safety precautions recommended by their manufacturers should be observed.

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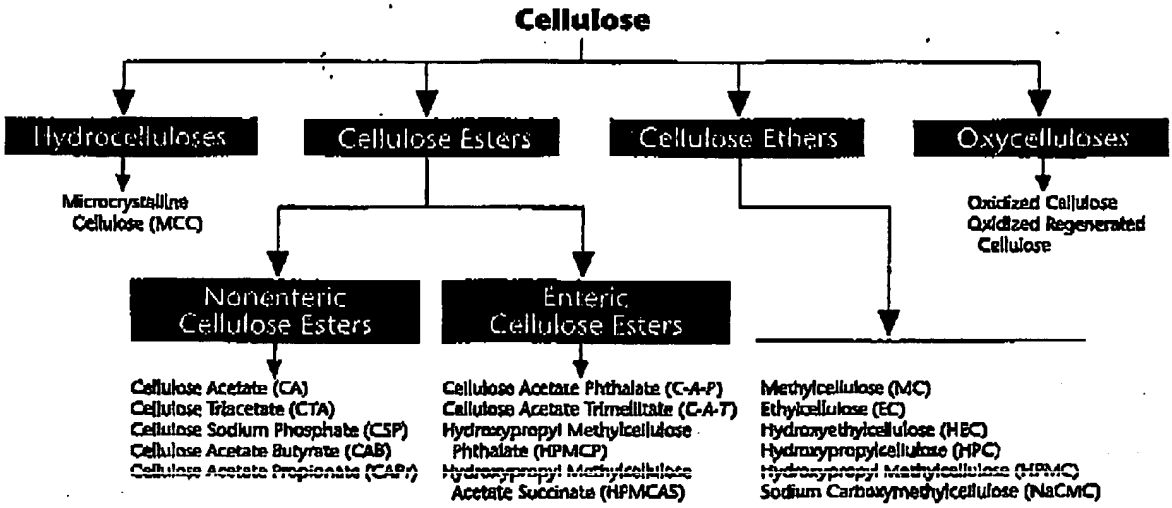
Figure 2
Cellulose Derivatives[a]



[a] *V. J. Kumar and G. Banker*

Cellulose Acetate

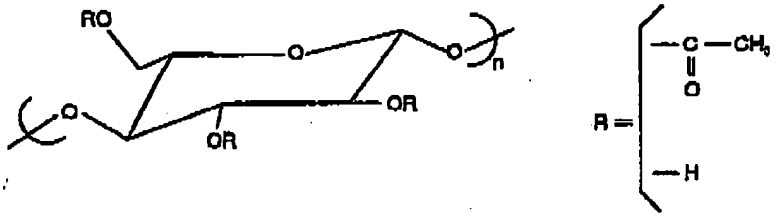


Table 1
Chemical Properties of Cellulose Acetate

Type	Viscosity,[a] cP	Acetyl, %	Combined Acetic Acid, %	Hydroxyl, %	Melting Range, °C	T_g, °C	Density, kg/L	MW_n
CA-320S	210.0	32.0	44.7	8.7	230–250	180	1.31	38,000
CA-398-3	11.4	39.8	55.5	3.5	230–250	180	1.31	30,000
CA-398-6	22.8	39.8	55.5	3.5	230–250	182	1.31	35,000
CA-398-10	38.0	39.8	55.5	3.5	230–250	185	1.31	40,000
CA-398-30	114.0	39.7	55.5	3.5	230–250	189	1.31	50,000
CA-394-60S	228.0	39.5	55.0	4.0	240–260	186	1.32	60,000
CA-435-75	—	43.5	60.6	0.9	280–300	185	1.31	122,000

[a] *ASTM D 817 (Formula A) and D 1343*